# Tocilizumab (Actemra®)

Tocilizumab is a recombinant humanized interleukin-6 (IL-6) receptor monoclonal antibody of the immunoglobulin IgG1K subclass. Two heavy chain and two light chain polypeptides are linked by intra- and inter-molecular disulfide bonds. Endogenous IL-6 is induced by inflammatory stimuli and mediates a variety of immunological responses. Inhibition of IL-6 receptors by tocilizumab leads to a reduction in cytokine and acute phase reactant production.

## Resources from Manufacturer

Patient Medication Guide
Full Prescribing Information
Dosing Calculator Dosing Calculator
Actemra Co-Pay Assistance Program
Genentech Patient Assistance Foundation

## Tocilizumab-aazg (Tyenne) Resources

Patient Medication Guide
Full Prescribing Information
Financial Assistance Programs

## Tocilizumab-bavi (Tofidence) Resources

Patient Medication Guide
Full Prescribing Information

## Indications and Dosing in Rheumatology

**Tocilizumab is indicated for:**

- Adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease Modifying Anti-Rheumatic Drugs (DMARDs)
- Active polyarticular juvenile idiopathic arthritis (PJIA) in patients two years of age and older
- Active systemic juvenile idiopathic arthritis (SJIA) in patients two years of age and older
- Adult patients with giant cell arteritis (GCA)
- Adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) to slow the rate of decline in pulmonary function

**Dosing:**

- **IV dosing:**
  - ❑ Tocilizumab is given as a 60-minute single intravenous drip infusion.
  - ❑ Doses exceeding 800 mg per infusion are not recommended for RA, while doses exceeding 600 mg per infusion are not recommended for GCA.
- **SC dosing:**
  - ❑ If transitioning from IV to SC therapy, administer the first subcutaneous dose instead of the next scheduled infusion.
  - ❑ Interruption of dose or reduction in dose frequency from every week to every other week may be needed for management of dose-related laboratory abnormalities including elevated liver enzymes, neutropenia, and thrombocytopenia.

## Indications and Dosing in Rheumatology *continued*

### Rheumatoid Arthritis (RA)

- Tocilizumab may be used as monotherapy or concomitantly with methotrexate or other non-biologic DMARDs as an IV infusion or subcutaneous injection.
- **IV dosage**
  - The recommended initial dosage is 4 mg/kg every 4 weeks followed by an increase to 8 mg/kg every 4 weeks based on clinical response.
- **SC dosage**

| Weight | Dosing |
|---|---|
| <100 kg | 162 mg every other week, followed by an increase to every week based on clinical response |
| ≥ 100 kg | 162 mg every week |

### Polyarticular Juvenile Idiopathic Arthritis (PJIA)

- Tocilizumab may be used alone or in combination with methotrexate.
- The recommended dosage given as IV infusion or SC injection is:

| Weight | Intravenous Dosing | Subcutaneous Dosing |
|---|---|---|
| < 30 kg | 10 mg/kg every 2 weeks | 162 mg every 2 weeks |
| ≥ 30 kg | 8 mg/kg every 2 weeks | 162 mg every week |

### Systemic Juvenile Idiopathic Arthritis (SJIA)

- Tocilizumab may be used alone or in combination with methotrexate.
- The recommended dose of tocilizumab given as an IV infusion or SC injection is:

| Weight | Intravenous Dosing | Subcutaneous Dosing |
|---|---|---|
| < 30 kg | 12 mg/kg every 2 weeks | 162 mg every 2 weeks |
| ≥ 30 kg | 8 mg/kg every 2 weeks | 162 mg every week |

### Giant Cell Arteritis (GCA)

- **IV dosage**
  - The recommended initial dosage is 6 mg/kg every 4 weeks in combination with tapering course of glucocorticoids, then alone following discontinuation of glucocorticoids.
- **SC dosage**
  - The recommended dosage is 162 mg every week in combination with a tapering course of glucocorticoids.
  - A dose of 162 mg every other week in combination with taper course of glucocorticoids may be prescribed based on clinical considerations.

### Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)

- The recommended dosage is 162 mg subcutaneously given once every.
- Intravenous administration is not FDA approved for SSc-ILD.

## Contraindications

Known hypersensitivity to tocilizumab

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## Warnings and Precautions

- Serious Infections–do not administer during an active infection. If a serious infection develops, interrupt tocilizumab until the infection is controlled.
- Gastrointestinal perforation n Hepatotoxicity–Monitor for marked elevations of transaminases (>5 times ULN), as well as mildly elevated transaminases in some cases.
- Hypersensitivity reactions including anaphylaxis and death.
- Active Hepatic disease and Hepatic impairment–use is not recommended
- Live vaccines–avoid use
- Pregnancy–may cause fetal harm
- Lactation–discontinue drug or nursing
- Laboratory monitoring–potential treatment-related changes in neutrophils, platelets, lipids and liver specific enzymes. Modify dosage to manage neutropenia, thrombocytopenia, and/or elevated liver transaminases:

| | Threshold | Recommendation |
|---|---|---|
| ANC | 500-1,000 cells/mm3 | Hold treatment with tocilizumab until ANC >1,000, then resume with consideration of modifying IV dose or SC dosing interval, then increase as clinically appropriate. |
| | <500 cells/mm3 | Discontinue tocilizumb |
| Platelets | 50,000-100,000 cells/mm3 | Hold treatment with tocilizumab until platelets >100,000, then resume with consideration of modifying IV dose or SC dosing interval, then increase as clinically appropriate. |
| | <50,000 cells/mm3 | Discontinue tocilizumab |
| ALT or AST | >ULN to ≤3x ULN | Consider dosage modification of concomitant DMARDs as clinically appropriate. |
| | 3x ULN to ≤5x ULN | Hold treatment with tocilizumab until ALT/AST < 3x ULN, then resume with consideration of modifying IV dose or SC dosing interval as clinically appropriate. |
| | >5x ULN | Discontinue tocilizumab |

## Adverse Reactions (≥ 5%)

- Upper respiratory tract infections
- Nasopharyngitis
- Headache
- Hypertension
- Increased ALT
- Injection site reactions

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## Medication Strength and Preparations

- Tocilizumab and tocilizumb-aazg single-dose pre-filled syringe: 162 mg/0.9 mL
- Tocilizumab and tocilizumb-aazg single-dose prefilled auto-injector: 162 mg/0.9 mL
- Tocilizumab, tocilizumab-aazg, and tocilizumab-bavi solution in single-dose vial (for IV infusion): 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL

## Medication Administration and Storage

- Store in original carton to protect from light
- Store in refrigerator at 2°C to 8°C (36°F to 46°F)–do not freeze
- Syringe and auto-injector safe at room temperature (defined as 20°C and 30°C (68°F and 86°F)) for up to 14 days

### Subcutaneous Administration

- Before injecting, allow injection to warm to room temperature for 30 – 90 minutes prior to administration
- Inject subcutaneously into front of thigh, lower abdomen (avoid injecting within 2 inches of navel), or outer area of upper arm
- Do not administer into tender, bruised, red or hard skin
- Rotate injection sites (≥ 1 inch apart)

## Intravenous Medication Preparation

1. Tocilizumab is supplied as a sterile, preservative-free solution for intravenous (IV) infusion in single use vials (80 mg/4 mL, 200 mg/10 mL and 400 mg/20mL).
2. Do not dilute vials until after successfully obtaining intravenous access.
3. For adults RA, PJIA and SJIA patients weighing at or above 30 kg, dilute to 100 mL in 0.9% (NS) or 0.45% (1/2 NS) NaCl for intravenous infusion using aseptic technique.
4. For PJIA and SJIA patients weighing less than 30 kg, dilute to 50 mL in 0.9% or 0.45% NaCl for intravenous infusion using aseptic technique.
5. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. If particulates and discoloration are noted, the product should not be used. Fully diluted tocilizumab solutions are compatible with polypropylene, polyethylene and polyvinyl chloride infusion bags and polypropylene, polyethylene and glass infusion bottles.
6. The fully diluted tocilizumab solutions for infusions can be stored at 36 – 46 degrees Fahrenheit for up to 24 hours if diluted in either NS or ½ NS, at room temperature for up to 24 hours if diluted in NS, or at room temperature for up to 4 hours if diluted in ½ NS. Vials should be protected from light.
7. Tocilizumab solution does not contain preservatives; therefore, unused product remaining in the vials should NOT be used.
8. Allow the fully diluted tocilizumab solution to reach room temperature prior to infusion.
9. The infusion should be administered over 60 minutes and must be administered with an infusion set. Do not administer as an intravenous push or bolus.
10. Tocilizumab should not be infused concomitantly in the same intravenous line with other drugs. No physical or biochemical compatibility studies have been conducted to evaluate the coadministration of tocilizumab with other drugs.

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## Managing Infusion Reactions

1. Acute infusion reaction can occur during the administration of tocilizumab or within 24 hours of infusion. If the patient reports mild reactions (such as flushing, chills, etc.), slow down the infusion rate and assess the patient. Notify the supervising provider of the reaction.
2. For more severe reactions (such as hives, difficulty breathing, chest pain, high or low blood pressure, swelling of face and hands, fever, chills or anaphylaxis) or when mild reactions persist despite slowing the infusion, stop the infusion and treat the acute reaction. Tocilizumab should not be given to patients who have experienced anaphylaxis or other severe hypersensitivity and not re-challenged.

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